UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,334	07/10/2003	Michael R. Hayden	760050-91	5209

7590 02/22/2007

CARELLA, BYRNE, BAIN, GILFILLAN, CECCHI,
STEWART & OLSTEIN
6 Becker Farm Road
Roseland, NJ 07068

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/617,334	HAYDEN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,29-42 and 46-62* is/are pending in the application.

4a) Of the above claim(s) *1-23,29-40,46-48 and 50-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,41,42,49 and 57-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-27, 29-42, and 46-62 are pending in the application.

[2] Applicant's amendment to the claims, filed on 11/14/06, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims. Applicant is reminded of the amendment practice according to 37 CFR 1.121, which requires markings to show changes made relative to the prior claim version. See, *e.g.,* claim 24, wherein the term "ABC1-mediated" appears to have been added without showing underlining and "ABCA1" appears to have been deleted without showing strikethrough.

[3] Applicant's amendment to the specification, filed on 11/14/06, is acknowledged.

[4] Receipt of a terminal disclaimer, filed on 11/14/06, is acknowledged.

[5] Receipt of an information disclosure statement, filed on 11/14/06, is acknowledged.

[6] Applicant's arguments filed on 11/14/06 have been fully considered and are deemed to be persuasive to overcome some of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[7] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[8] Claims 1-23, 29-40, 46-48, and 50-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/6/2006.

[9] Claims 49, 58, and 60 are being examined only to the extent the claims read on the elected subject matter.

Information Disclosure Statement

[10] With the exception of references Y2, Z2, and A3, all references cited in the information disclosure statement filed on 11/14/06 have been considered by the examiner. A copy of Form PTO-1449 is attached to the instant Office action. References Y2, Z2, and A3 have not been considered as a copy of these references has not been provided in accordance with 37 CFR 1.98(2).

Claim Rejections - 35 USC § 112, Second Paragraph

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[11] Claim(s) 24-27, 41-42, 49, and 57-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "increase HDL-C" and "increases ABC1-mediated lipid transport activity" in claim 24 (claims 26-27, 41-42, 49, and 57-62 dependent therefrom) and "low

HDL-C" in claim 25 are unclear absent a statement defining to what the levels of HDL-C or ABC1-mediated lipid transport activity are being compared. The terms "increase HDL-C," "increases ABC1-mediated lipid transport activity," and "low HDL-C" are relative terms and the claims should define and clearly state as to what the levels of HDL-C or ABC1-mediated lipid transport activity is being compared.

Claim Rejections - 35 USC § 112, First Paragraph

[12] Claims 24-27, 41-42, 49, and 57-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims." MPEP § 2163 further states, "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description." Claim 24 recites the limitation "[a] method...to increase HDL-C...ABC1-mediated lipid transport activity" (emphasis added). Applicant points to p. 75, lines 20-24 as showing support for the recited limitation. This disclosure is related to subtyping ABC1 gene and its use to subtype low HDL individuals and is not

related to increasing HDL-C or ABC1-mediated lipid transport activity. According to the specification, ABC1 biological activity includes lipid transport activity (specification at paragraph bridging pp. 55-56, see particularly p. 56, line 6). However, the examiner can find no support in the original application for a method for increasing HDL-C by increasing ABC1-mediated lipid transport activity. Also, it is noted that ABC1-*mediated* lipid transport activity is a limitation that is broader than ABC lipid transport activity, since an activity that is "mediated" by ABC1 need not be an activity of ABC1 itself. As such, it is the examiner's position that the limitation as noted above is new matter.

Also, claim 25 recites the limitation "cardiovascular disease is associated with low HDL-C." Applicant points to p. 75, lines 20-24, p. 1, line 26, and p. 76 as showing support for this limitation. However, while the examiner can find support for *risk* of cardiovascular disease being correlated with low HDL-C, the examiner can find no explicit, implicit, or inherent disclosure in the original application that supports the broader limitation of cardiovascular disease being *associated* with low HDL-C.

Applicant is invited to show support for the limitations of new claims 57-62.

[13] The written description rejection of claims 24-27, 41-42, 49, and 57-62 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record (paragraph 14 beginning at p. 6 of the 5/31/06 Office action) and the reasons set forth below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant notes the written description requirement may be satisfied by adequately describing the properties of an

embodiment, without disclosing specific embodiments themselves, citing *Union Oil Co. of California v. Atlantic Richfield Co.* (54 USPQ2d 1227). Applicant argues the instant case is different from *University of Rochester v. G.D. Searle and Co.* (69 USPQ2d 1886) because the claims of the *Rochester* case "were drawn to a method of selectively inhibiting PGHS-2 activity by administering a compound that selectively inhibits such activity (which is tautomeric)." Applicant argues amended claim 24 describes how to use an agent that increases lipid transport activity of ABC1 and there is provided a means for identifying such agents, citing claims of the issued parent application as evidence thereof. Thus, according to applicant, a skilled artisan would recognize how to find such modulators and how to use them, which satisfies the written description requirement.

Applicant's argument is not found persuasive. The claims are drawn to a method of treating a mammal using a genus of compounds that increase ABC1-mediated lipid transport activity, wherein the genus of compounds is defined in the claim solely by recitation of a functional feature. Although neither the specification nor the prior art appears to recognize a compound as encompassed by claim 24 – which is undisputed by applicant – applicant appears to take the position that because the specification teaches how to screen for such compounds and how to use them, the genus of compounds that increase ABC1-mediated lipid transport activity are adequately described. Although applicant relies on *Union Oil Co. of California v. Atlantic Richfield Co.*, the facts of the *Union* case appear to be inapposite to the instant case, because in *Union,* the "components" of the gasoline were not at issue. *Union* did not require experimental screening and testing to isolate the "components" used in their gasoline. In

contrast to *Union*, the compounds used in the claimed methods are neither disclosed in the specification nor do they appear to have been known in the prior art. Applicant takes the position that, by teaching "how to find such modulators and exactly what to do with them," the genus of compounds is adequately described, even though the specification fails to describe the structure of even a single representative species of the genus of compounds as recited in claim 24.

Although applicant argues *Rochester* does not apply here, the facts of *Rochester* are highly analogous to this case. In *Rochester,* the Court held that, although the specification teaches methods for screening for the compounds used in the claimed methods, the specification nonetheless failed to disclose "just 'which 'peptides, polynucleotides, and small organic molecules' have the desired characteristic of selectively inhibiting PGHS-2'" since "[n]o compounds that will perform the claimed method are disclosed, nor has any evidence been shown that such a compound was known" (emphasis original; *Id* at 18). Similarly, no compounds that will perform the method of the claims are disclosed and there is no evidence of record that such a compound was known at the time of the invention. It is acknowledged that applicant states "some upregulators of ABC1 are disclosed in the application at page 55, lines 14-16" (instant response at p. 23, middle) and "clearly analogs of cholesterol and HDL are likely starting points" in identifying ABC1-mediated lipid transport activity agonists (instant response at p. 20, middle). However, there is no evidence of record that the compounds as disclosed at p. 55, lines 14-16 have the desired activity of increasing ABC1-mediated lipid transport activity, particularly as applicant concedes "there may be

many compounds that modulate some kind of ABC1 activity but modulating an activity like HDL-C transport is much more specific" and suggests that further experimentation is required to identify such compounds (instant response at p. 21, top). According to MPEP 2163.I, "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention" (citation omitted). Because the specification fails to disclose even a single representative species of the recited genus of compounds, the examiner maintains that a skilled artisan would not conclude that applicant was in possession of the claimed invention.

[14] The scope of enablement rejection of claims 24-27, 41-42, 49, and 57-62 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record (paragraph 15 beginning at p. 6 of the 5/31/06 Office action) and the reasons set forth below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Regarding the breadth of the claims, applicant argues claim 24 has been amended to recite increasing the lipid transport activity of ABC1 and not just any biological activity.

While the examiner acknowledges the amendment to claim 24, the claims remain overly broad with respect to the scope of compounds that "increase[] ABC1-mediated lipid transport activity in said mammal." As noted in the prior Office action and undisputed by applicant – the scope of compounds encompasses (but is not necessarily limited to) any small organic compound, any peptide or polypeptide including an

antibody, and a nucleic acid. Further, it is noted that the scope of compounds is not limited to those that increase ABC1-mediated lipid transport by direct interaction with ABC1, but broadly encompasses compounds that indirectly increase ABC1-mediated lipid transport, *e.g.,* a compound that enhances the level of a transcription factor that upregulates ABC1 mRNA (see specification at p. 51, lines 26-31).

Addressing the state of the art/level of skill/predictability, applicant argues that because ABC1 has a disclosed physiological role on HDL-C levels, then "clearly analogs of cholesterol and HDL are likely starting points" in identifying ABC1-mediated lipid transport activity agonists (instant response at p. 20, middle). According to applicant, due to advances in combinatorial chemistry and screening assays, "numerous" compounds can be identified for use in the claimed method.

There is no dispute that the state of the art regarding combinatorial chemistry and screening assays was advanced at the time of the invention. However, because there was no disclosure or evidence of a compound as encompassed by claim 24 at the time of the invention, a skilled artisan would have recognized the high level of unpredictability in isolating such a compound – if at all it existed or could be produced. As noted in the prior Office action, even after the time of the invention the art recognizes that therapies targeting ABCA1 for the treatment of coronary heart disease "has not yet been fulfilled" (Nofer et al. *Cell Mol Life Sci* 62:2150-2160, 2005; p. 2156, right column, bottom).

Regarding the amount of direction and guidance/working examples, applicant argues the specification discloses the relationship between ABC1 and HDL-C transport

and further discloses screening assays for identifying compounds as encompassed by the claims.

The examiner does not dispute the disclosure of certain screening assays as noted by applicant at p. 18, paragraphs 2-4 of the instant response. However, disclosure of screening assays is insufficient to guide a skilled artisan to a particular compound having a particular activity, particularly, as applicant notes, "there may be many compounds that modulate some kind of ABC1 activity but modulating an activity like HDL-C transport is much more specific" (instant response at p. 21, top) and would require additional experimentation to identify such compounds. In this case, the specification and/or prior art fail to disclose even a single working example of the recited compound, and while applicant asserts that numerous such compounds can be identified using combinatorial methods and screening assays, there is no evidence to support such an assertion. Further, even if a skilled artisan could make a compound having the recited function of increasing ABC1-mediated lipid transport activity to increase HDL-C, the scope of claims is unlimited and neither the specification nor the prior art provides guidance regarding, *e.g.*, the type(s) of compound (small organic, peptide, polypeptide, nucleic acid), that are likely to have such activity from those that are not. While the examiner acknowledges that the requirements for an enabling disclosure do not require disclosure of a working example, MPEP 2164.02 states "[l]ack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art." In view of the teachings of Nofer et al. as noted above and because there is no evidence of a compound as recited in the

claims, it is the examiner's position that the art regarding a compound that increases ABC1-mediated lipid transport activity in a mammal is both unpredictable and underdeveloped and thus, the lack of a working example is a factor that has been considered in evaluating the enablement provided by the specification's disclosure.

Addressing the quantity of experimentation, applicant argues claim 24 has been amended to limit the ABC1-mediated biological activity to increasing ABC1-mediated lipid transport activity to increase HDL-C. According to applicant, by disclosing the specific activity to be modulated and the disease to be treated or prevented, this is sufficient for a skilled artisan to "quickly generate useful materials for carrying out the invention."

While applicant takes the position that based on the disclosure one can "quickly" produce compounds as encompassed by the claims. However, this appears to be mere speculation, particularly as neither the specification nor the prior art discloses a single compound that has the function of increasing ABC1-mediated lipid transport activity resulting in increased HDL-C in a mammal. Because the specification and prior art fail to provide a working example of such a compound and thus an expectation that such compound can be made, it cannot be predicted *a priori* that the experimentation required to make such compounds can be practiced "quickly." It is the examiner's position that, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the significant amount of non-routine experimentation required, undue experimentation

would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

[15] The rejection of claim(s) 24-28 and 42 under 35 U.S.C. 102(a) or 35 U.S.C. 102(e) as being anticipated by Whitcomb (US Patent 5,859,037; hereafter, Whitcomb '037) as evidenced by Nieland et al. (*J Lipid Res* 45:1256-1265, 2004); the rejection of claim(s) 24-28, 42-43, 45, and 57-62 under 35 U.S.C. 102(a) or 35 U.S.C. 102(e) as being anticipated by Whitcomb '037 as evidenced by Nieland et al. and further evidenced by Whitcomb (US Patent 5,972,973, hereafter Whitcomb '973); the rejection of claim(s) 24-28, 42, and 49 under 35 U.S.C. 102(a) or 35 U.S.C. 102(e) as being anticipated by Whitcomb '037 as evidenced by Nieland et al. and further evidenced by Cooper et al. (US Patent 5,260,275); and the rejection of claims 24-26, 28, 41, 43-44, 57-60, and 62 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kamei et al. (*Psychopharmacology* 113:318-321, 1994) as evidenced by Nieland et al. and Whitcomb '973 are withdrawn in view of the amendment to claim 24 to require that the compound increase ABC1-mediated lipid transport activity in a mammal. As noted in the prior Office action, the treatment compound used in the prior art, *i.e.,* glyburide, appears to decrease ABC1-mediated cholesterol efflux. As such, the compound used in the prior art references would not have the recited activity and thus the prior art references teaching administration of glyburide do not teach all limitations of the claims.

[16] Claim(s) 24-27, 42, 49, and 59-60 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Smud et al. (*Curr Med Res Opin* 10:612-624, 1987) as evidenced by Steiner et al. (*Diabetologia* 39:1655-1661, 1996) and Arakawa et al. (*Arterioscler Thromb Vasc Biol* 25:1193-1197, 2005). The claims are drawn to a method for treating a mammal having or at risk of developing a cardiovascular disease to increase HDL-C by administering to said mammal a compound that increases ABC1-mediated lipid transport activity.

The reference of Smud et al. teaches a method of administering fenofibrate in combination with glibenclamide or chlorpropamide to diabetic patients (pp. 613-615). According to Smud et al., "[t]here is an increased risk in diabetic patients of morbidity or mortality due to ischaemic coronary vascular disorders...this risk was related to low HDL cholesterol concentrations" (p. 621, top). Smud et al. teaches that treatment resulted in a "significant" increase in HDL cholesterol levels (paragraph bridging pp. 616-617).

Evidentiary references Steiner et al. and Arakawa et al. are cited in accordance with MPEP 2131.01 as showing that a characteristic not disclosed in the reference of Smud et al. is inherent. Steiner et al. discloses "[t]he frequency of coronary artery disease is greatly increased in diabetic patients" (p. 1655, left column, middle). Evidentiary reference Arakawa et al. is cited in accordance with MPEP 2124 as showing that treatment of cells with fenofibrate results in increased ABC1 mRNA and protein levels (p. 1194, paragraph bridging left and right columns). Increased levels of ABC1

protein would result in increased ABC1-mediated lipid transport activity. Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (*i.e.,* that the method of the prior art does not have the same result of increasing ABC1-mediated lipid transport activity as that of the claimed method). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[17] Claim(s) 24-27, 42, 49, and 57-62 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hahmann et al. (*Am J Cardiol* 67:957-961, 1991) as evidenced by Arakawa et al. (*Arterioscler Thromb Vasc Biol* 25:1193-1197, 2005). The claims are drawn to a method for treating a mammal having or at risk of developing a cardiovascular disease to increase HDL-C by administering to said mammal a compound that increases ABC1-mediated lipid transport activity.

The reference of Hahmann et al. discloses a study on the effects of fenofibrate on patients with coronary artery disease (pp. 957-959, particularly p. 957, abstract, top). According to Hahmann et al., treatment with fenofibrate increased HDL-cholesterol by 19% (p. 957, abstract).

Evidentiary reference Arakawa et al. is cited in accordance with MPEP 2131.01 and MPEP 2124 as showing that a characteristic not disclosed in the reference of Hahmann et al. is inherent. Evidentiary reference Arakawa et al. is cited as showing that

treatment of cells with fenofibrate results in increased ABC1 mRNA and protein levels (p. 1194, paragraph bridging left and right columns). Increased levels of ABC1 protein would result in increased ABC1-mediated lipid transport activity. Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (*i.e.*, that the method of the prior art does not have the same result of increasing ABC1-mediated lipid transport activity as that of the claimed method). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[18] Claim(s) 24-27, 41, 49, and 59-60 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Olivier et al. (*Atherosclerosis* 70:107-114, 1988) as evidenced by Mack et al. (*Am J Public Health* 81:1180-1184, 1991) and Arakawa et al. (*Arterioscler Thromb Vasc Biol* 25:1193-1197, 2005). The claims are drawn to a method for treating a mammal having or at risk of developing a cardiovascular disease to increase HDL-C by administering to said mammal a compound that increases ABC1-mediated lipid transport activity.

The reference of Olivier et al. teaches a method of administering fenofibrate in mice receiving a hypercholesterolemic diet, including added cholesterol (p. 108, left and right columns and p. 110, Table 2). According to Olivier et al., treatment with fenofibrate resulted in a 23% increase in HDL-C as compared to mice not receiving fenofibrate (p. 110, Table 2).

Evidentiary references Mack et al. and Arakawa et al. are cited in accordance with MPEP 2131.01 as showing that a characteristic not disclosed in the reference of Olivier et al. is inherent. Mack et al. teaches a correlation between high plasma cholesterol levels and the incidence of coronary artery disease (p. 1180, abstract) and thus, the mice receiving the hypercholesterolemic diet would be considered to be at risk for developing coronary artery disease. Evidentiary reference Arakawa et al. is cited in accordance with MPEP 2124 as showing that treatment of cells with fenofibrate results in increased ABC1 mRNA and protein levels (p. 1194, paragraph bridging left and right columns). Increased levels of ABC1 protein would result in increased ABC1-mediated lipid transport activity. Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (*i.e.,* that the method of the prior art does not have the same result of increasing ABC1-mediated lipid transport activity as that of the claimed method). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Claim Rejections - Double Patenting

[19] The provisional obviousness-type double patenting rejection of claims 24-28, 41-45, 49, and 57-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-45 of co-pending US non-provisional

application 10/744,465 is withdrawn in view of applicant's submission of a terminal disclaimer filed on 11/14/06.

[20] The provisional obviousness-type double patenting rejection of claims 24-28, 41-45, 49, and 57-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-24 and 26-27 of co-pending US non-provisional application 10/479,198; the provisional obviousness-type double patenting rejection of claims 24-28, 41-45, 49, and 57-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-28 and 32 of co-pending US non-provisional application 10/745,377; and the provisional obviousness-type double patenting rejection of claims 24-28, 41-45, 49, and 57-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-48 of co-pending US non-provisional application 10/833,679 are maintained for the reasons of record and the reasons set forth below. The rejections were fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Regarding the provisional rejections over the '198 and '377 applications, applicant argues the provisional rejections are obviated in view of the filing of terminal disclaimers. The examiner has made an earnest attempt to locate said terminal disclaimers. However, the examiner no such terminal disclaimers can be located in the application file.

Regarding the provisional rejection over the '679 application, applicant argues the claims of the '679 application recite administering a nucleic acid encoding ABC1,

which would encode more ABC1 polypeptide, whereas the instant claims are drawn to the use of compound that increases ABC1-mediated lipid transport activity.

Applicant's argument is not found persuasive. One of ordinary skill in the art would recognize that, broadly interpreted, administering an ABC1-encoding nucleic acid would result in an increase in levels of ABC1 polypeptide and would have the resulting effect of increasing ABC1-mediated lipid transport activity due to the increase level of ABC1 protein. As such, the compound of the claims of the '679 application is encompassed by the instant claims.

Conclusion

[21] Status of the claims:

- Claims 1-27, 29-42, and 46-62 are pending.
- Claims 1-23, 29-40, 46-48, and 50-56 are withdrawn from consideration.
- Claims 24-27, 41-42, 49, and 57-62 are rejected.
- No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656